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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,898	09/23/2004	Linda L. Brockunier	21070YP	3656
210 7590 06/28/2007 MERCK AND CO., INC P O BOX 2000 RAHWAY, NJ 07065-0907			EXAMINER LOEWE, SUN JAE Y	
			ART UNIT 1609	PAPER NUMBER
			MAIL DATE 06/28/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/508,898

Applicant(s)

BROCKUNIER ET AL.

Examiner

Sun Jae Y. Loewe

Art Unit

1609

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-7, 9, 12, 13, 15, 16, 18-21, 24 and 42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-7, 9, 12, 13, 15, 16, 18-21, 24 and 42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 2-7, 9, 12, 13, 15, 16, 18-21, 24, and 42 are currently pending in the instant application and are rejected.

Response to Amendment

2. Applicant's amendment to the claims has overcome the following rejection/objection: (a) 35 USC 112 1st paragraph rejection of claims 2-7, 9, 12, 13, 15, 16, 18-21 and 24; (b) objection to claim 20.
3. Applicant's amendment to the specification has overcome the objection to the abstract.
4. The allowability of subject matter indicated in the previous office action is withdrawn in view of the following sections 6-8.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The term "controlling" in claim 24 is a relative term which renders the claim indefinite. The term "controlling" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. First, it is not clear what is meant by the term as applied towards a disease or condition. A multitude of meanings can be envisioned, for example, lessening the symptoms, delaying the onset, etc. Second, given a precise meaning for the term, it

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is still unclear as to what degree or against what standard the “control” is measured. This claimed limitation was not examined herein because the meaning could not be delineated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
 2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
6. (i) Claims 2-7, 9, 12, 13, 15, 16, 18-21, 24 and 42 rejected under 35 U.S.C. 103(a) as being obvious over Edmonson et al., US 6,699,871. See for example, examples 1-11, 17-27, 30 and 31 (columns 25, 27, 28, 29, 30, 32, 33).
- (ii) Claims 2-7, 9, 12, 13, 15, 16, 18-21, 24 and 42 rejected under 35 U.S.C. 103(a) as being obvious over Edmonson et al., US 7,125,873. See for example, examples 1-11, 17-27, 30 and 31 (columns 26, 27, 28, 29, 30, 31, 32, 33).
- (iii) Claims 2-7, 9, 12, 13, 15, 16, 18-21, 24 and 42 rejected under 35 U.S.C. 103(a) as being obvious over Edmonson et al., US2006/0270679. See for example, examples 1-11, 17-27, 30 and 31 (pages 14, 15, 16, 17, 18).

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The applied references have common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Determination of the scope and contents of the prior art.

All three references teach exactly the same compounds: i.e. compounds shown in Scheme 1b and 1d.

Ascertaining the differences between the prior art and the claims at issue.

The prior art compounds have been excluded from the instantly claimed genus (Scheme 1a and 1c) via the proviso that R₅ and R₆ cannot both be hydrogen.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

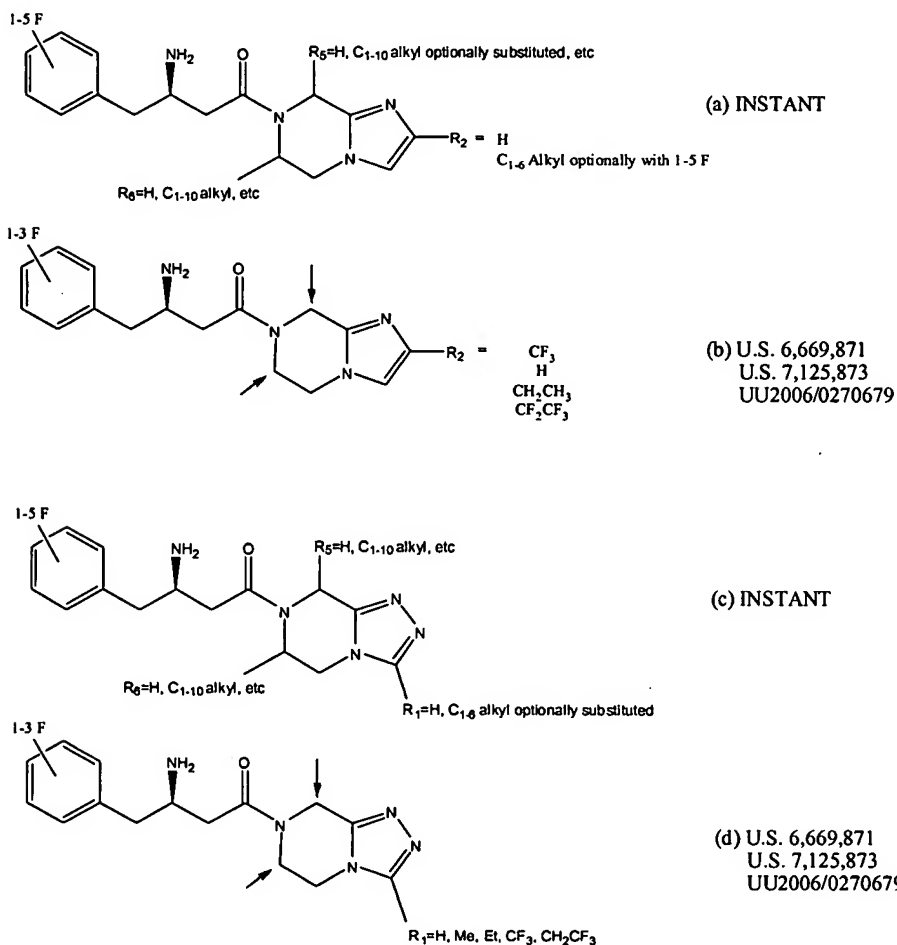
One of ordinary skill in possession of any of the three references would be motivated to make the following compounds, with reasonable expectation of obtaining the same DP-IV inhibition activity: homologs of the compounds in Scheme 1b and 1d wherein either of the two positions marked by the arrows are substituted with alkyl. These homologous compounds fall within the genus instantly claimed. Thus, based on structural similarity, the prior art suggests to one of ordinary skill in the art to make this substitution. A *prima facie* case of obviousness based on structure exists if the prior art suggest to one of ordinary skill in the art to make the substitution or modification. *In re Taborsky* (CCPA 1974) 502 F2d 775, 183 UPQ 50. Thus, the instant claims are *prima facie* obvious over the teachings of the three references. To those skilled in chemical art, one homologue is

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not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. In re Henze, 85 USPQ 261 (1950). Additionally, the instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as DP-IV inhibitors.

Therefore, the instant claimed compounds would have been suggested to one skilled in the art. Additionally, it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (ie., a DP-IV inhibitor).

SCHEME 1



Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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7. (i) Claims 2-7, 9, 12, 13, 15, 16, 18-21, 24 and 42 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4-15, 18 and 23 of U.S. Patent No. 6,699,871. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons below.
- (ii) Claims 21 and 24 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 7,125,873. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons below.

Determining the scope and contents of the claims in (i) U.S. 6,699,871 and (ii) U.S. 7,125,873

(i) Claims are drawn to a genus of DP-IV inhibitors, pharmaceutical compositions thereof, and method of use to treat diabetes type 2. Preferred embodiments are compounds shown in Scheme 1b and 1d (species 1-11, 17-27, 30 and 31 listed in claim 15 of U.S. 6,699,871).

(ii) Claims drawn to composition comprising compound shown in Scheme 1d ($R_1=CF_3$) and method of treating diabetes type 2:

Ascertaining the difference between instant claims and the claims in (i) U.S. 6,699,871 and (ii) U.S. 7,125,873

(i) The instant claims are drawn to the genus of compounds shown in Scheme 1a and 1c, pharmaceutical compositions thereof, and method of use to treat diabetes. The claimed embodiments of U.S. 6,699,871, namely compounds in Scheme 1b and 1d (and pharmaceutical compositions and method of use thereof), are excluded from the instant claims by a proviso (i.e. R_5 and R_6 cannot both be hydrogen).

(ii) The instant claims are drawn to pharmaceutical compositions comprising compounds shown in Scheme 1a and 1c, and method of use to treat diabetes. The claimed subject matter of U.S. 7,125,873, namely pharmaceutical composition and method of use of compound in Scheme 1d, $R_1=CF_3$ is excluded from the instant claims by a proviso (i.e. R_5 and R_6 cannot both be hydrogen).

Resolving the level of ordinary skill in the art – prima facie obviousness

See discussion in Section 6, last paragraph (obviousness due to structural similarity for homologs). For the same reasons, the instant claims are *prima facie* obvious over the claims in US. 6,699,871 and U.S. 7,125,873.

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8. Claims 2-5, 9, 12, 13, 18-21, 24 and 42 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 11-14, 17-23 and 26 of copending Application No. 10,540,283 (US2006/0052382). Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons below.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Determining the scope and contents of the claims copending Appl No. 10,540,283

Claims are drawn to a genus of DP-IV inhibitors, pharmaceutical compositions thereof, and method of use to treat diabetes type 2. Preferred embodiments are compounds shown in Scheme 2b-d.

Ascertaining the difference between instant claims and the claims in copending Appl No. 10,540,283

The instant claims are drawn to the genus of compounds shown in Scheme 1a, pharmaceutical compositions thereof, and method of use to treat diabetes 2.

Scheme 2b: the next lower homolog of this compound, wherein one methyl substituent to the pyrazine ring is replaced by a hydrogen, falls within the genus of the instant claims. The claims of copending Appl. No. 10,540,283 drawn to this homolog (pharmaceutical compositions thereof and its use to treat diabetes II) would anticipate the instant claims.

Scheme 2c: a positional isomer of this compound, wherein the methyl substituents attach to the pyrazine ring at the positions that correspond to R₅ and R₆, falls within the genus of the instant claims. The claims of copending Appl. No. 10,540,283 drawn to this positional isomer (pharmaceutical compositions thereof and its use to treat diabetes 2) would anticipate the instant claims.

Scheme 2d: a positional isomer of this compound, wherein the methyl substituent attaches to the pyrazine ring at either of positions R₅ or R₆, falls within the genus of the instant claims. The claims of copending Appl. No. 10,540,283 drawn to this positional isomer (pharmaceutical compositions thereof and its use to treat diabetes 2) would anticipate the instant claims.

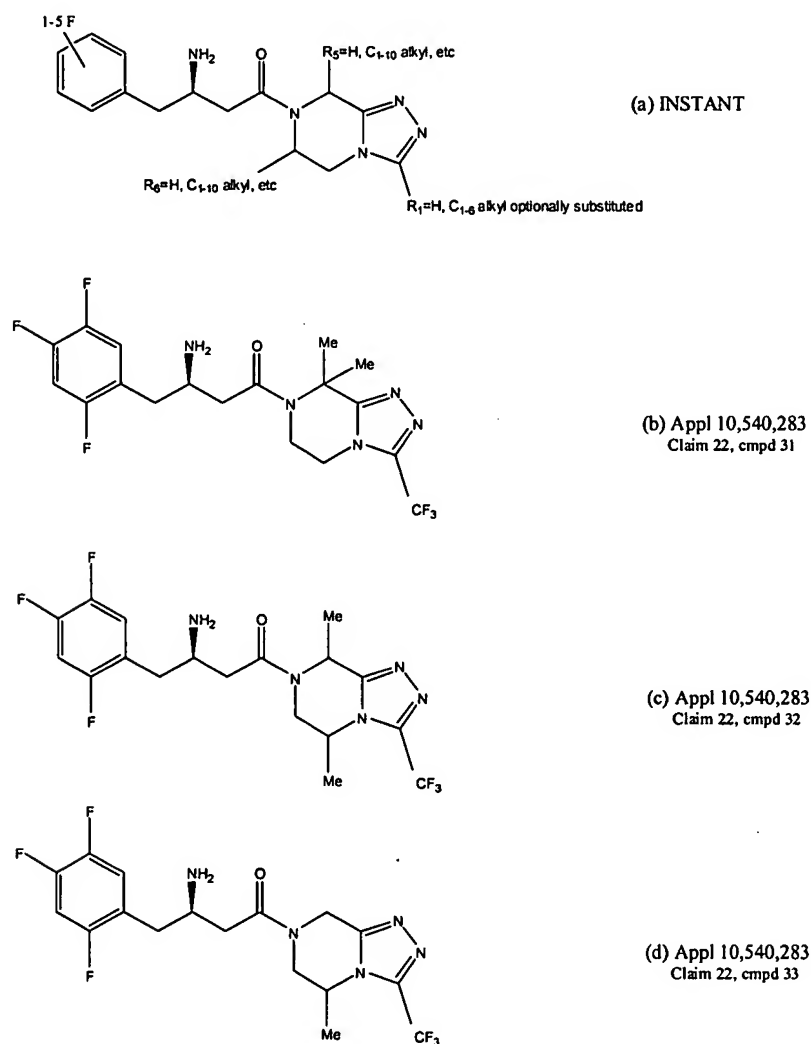
Resolving the level of ordinary skill in the art – prima facie obviousness

One of ordinary skill would be motivated, from the claims in copending Appl. No. 10,540,283, to make the modifications described above with reasonable expectation of

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obtaining the same DP-IV inhibition activity. Position isomers, and homologs, are generally of sufficiently close structural similarity that there is a presumed expectation that such compound possess similar properties. MPEP §2144.09, *Ex parte Henkel* 130 USPQ 474, (1-phenyl-3-methyl-4-hydroxypyrazole obvious over reference teaching 3-phenyl-5-methyl-4-hydroxypyrazole). *Ex parte Weston*, 121 USPQ 429. Thus, the instant claims are *prima facie* obvious over the claims in copending Appl. No. 10,540,283.

SCHEME 2



Conclusion

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9. No claims are allowed.

10. Any inquiry concerning this communication should be directed to Sun Jae Y. Loewe, Ph.D. whole telephone number is 571-272-9074. The examiner can normally be reached on Monday through Friday from 7:30 am to 5:00 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Cecilia Tsang (571) 272-0562, can be reached. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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